

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A polypeptide, ~~which has~~ having a binding affinity for HER2, ~~and which is related to a domain of staphylococcal protein A (SPA) in that~~ wherein the sequence of the polypeptide ~~corresponds to~~ comprises the sequence of the a protein Z derived from domain B of staphylococcal protein A (SPA), as set forth in SEQ ID NO:1 SPA domain, having from 1 to about 20 substitution mutations thereon.

2. (Previously Presented) A polypeptide according to claim 1, which has a binding affinity for HER2 such that the K_D value of the interaction is at most 1×10^{-6} M.

3. (Previously Presented) A polypeptide according to claim 2, which has a binding affinity for HER2 such that the K_D value of the interaction is at most 1×10^{-7} M.

4. (Canceled).

5. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising from 4 to about 20 substitution mutations.

6. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising substitution mutations at one or more of the
positions 13, 14, 28, 32 and 35.

7. (Previously Presented) A polypeptide according to claim
6, additionally comprising substitution mutations at one or more
of the positions 9, 10, 11, 17, 18, 24, 25 and 27.

8. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 13 from
phenylalanine to tyrosine.

9. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 14 from
tyrosine to tryptophan.

10. (Currently Amended) A polypeptide according to claim 1
~~claim 4-4-9~~, comprising a substitution mutation at position 28
from asparagine to an amino acid residue selected from arginine
and histidine.

11. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 28 from
asparagine to arginine.

12. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 32 from
glutamine to arginine.

13. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 35 from
lysine to tyrosine.

14. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 10 from
glutamine to arginine.

15. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 11 from
asparagine to threonine.

16. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 17 from
leucine to valine.

17. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, comprising a substitution mutation at position 27 from
arginine to an amino acid residue selected from lysine and
serine.

18. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, ~~the amino acid sequence of which corresponds to that of~~
~~SEQ ID NO:1~~, comprising at least the following mutations: F13Y,
Y14W, N28R, Q32R and K35Y.

19. (Currently Amended) A polypeptide according to claim 1
~~claim 4~~, the amino acid sequence of which is selected from the
group consisting of as set out in any one of SEQ ID NO:2-79.

20. (Currently Amended) A polypeptide according to claim 19,
the amino acid sequence of which is selected from the group
consisting of as set out in any one of SEQ ID NO:2-3.

21. (Currently amended) A polypeptide according to claim 1, in which at least one of the asparagine residues present in the protein Z derived from domain B of staphylococcal protein A (SPA) ~~to which said polypeptide is related~~ has been replaced with another amino acid residue.

22. (Currently Amended) A polypeptide according to claim 21, ~~the sequence of said domain of staphylococcal protein A (SPA) corresponding to the sequence of SPA protein Z as set forth in SEQ ID NO:1, and the polypeptide~~ comprising substitution mutations at at least one position chosen from N3, N6, N11, N21, N23, N28, N43 and N52.

23. (Previously Presented) A polypeptide according to claim 22, comprising at least one of the following mutations: N3A, N6A, N6D, N11S, N23T, N28A and N43E.

24. (Previously Presented) A polypeptide, which constitutes a fragment of a polypeptide according to claim 1, which fragment retains binding affinity for HER2.

25. (Previously Presented) A polypeptide according to claim 1, which comprises additional amino acid residues at either terminal.

26. (Previously Presented) A polypeptide according to claim 25, in which the additional amino acid residues comprise a cysteine residue at the N- or C-terminal of the polypeptide.

27. (Previously Presented) A polypeptide according to claim 25, in which the additional amino acid residues comprise a tag, preferably chosen from a hexahistidiny l tag, a myc tag and a flag tag.

28. (Currently Amended) A polypeptide according to claim 25, in which the additional amino acid residues comprise at least one functional polypeptide domain, so that the polypeptide is a fusion polypeptide between a first moiety, consisting of the polypeptide according to claim 1, and at least one ~~second and optionally~~ further moiety ~~or moieties~~.

29. (Currently Amended) A polypeptide according to claim 28, in which the ~~second~~ further moiety consists of one or more polypeptide(s) according to claim 1, making the polypeptide a

multimer of HER2 binding polypeptides according to claim 1, the sequences of which may be the same or different.

30. (Currently Amended) A polypeptide according to claim 28, in which the ~~second~~ further moiety comprises at least one polypeptide domain capable of binding to a target molecule other than HER2.

31. (Currently Amended) A polypeptide according to claim 30, in which the ~~second~~ further moiety comprises at least one polypeptide domain capable of binding to human serum albumin.

32. (Previously Presented) A polypeptide according to claim 31, in which the at least one polypeptide domain capable of binding to human serum albumin is the albumin binding domain of streptococcal protein G.

33. (Currently Amended) A polypeptide according claim 30, in which the ~~second~~ further moiety comprises a polypeptide which is related to a domain of staphylococcal protein A (SPA) in that the sequence of the polypeptide corresponds to the sequence of the SPA domain having from 1 to about 20 substitution mutations.

34. (Currently Amended) A polypeptide according to claim 33, in which the sequence of the ~~second~~ further moiety polypeptide comprises ~~corresponds to~~ the sequence of SPA protein Z derived from domain B of SPA, as set forth in SEQ ID NO:1, having from 1 to about 20 substitution mutations.

35. (Currently Amended) A polypeptide according to claim 28, in which the ~~second~~ further moiety is capable of enzymatic action.

36. (Currently Amended) A polypeptide according to claim 28, in which the ~~second~~ further moiety is capable of fluorescent action.

37. (Currently Amended) A polypeptide according to claim 28, in which the ~~second~~ further moiety is a phage coat protein ~~or a fragment thereof~~.

38. (Currently Amended) A polypeptide according to claim 1, which further comprises a label group.

39. (Currently Amended)) A polypeptide according to claim 38, in which the label group is ~~chosen~~ selected from the group consisting of fluorescent labels, biotin and radioactive labels.

40. (Previously Presented) A polypeptide according to claim 1, coupled to a substance having an activity against cells overexpressing HER2.

41. (Currently Amended) A polypeptide according to claim 40, in which said substance having an activity against cells overexpressing HER2 is ~~chosen~~ selected from the group consisting of cytotoxic agents, radioactive agents, ~~ADEPT~~ enzymes for antibody-directed enzyme prodrug therapy applications (ADEPT), cytokines and procoagulant factors.

42. (Cancelled).

43. (Cancelled).

44. (Cancelled).

45. (Canceled).

46. (Canceled).

47. (Previously Presented) A method of treatment of at least one form of cancer characterized by overexpression of HER2, which method comprises administering to a subject in need of such treatment a therapeutically effective amount of a composition, which comprises a polypeptide according to claim 1 as an active substance.

48. (Canceled).

49. (Previously Presented) A method of directing a substance having an anti-cancer activity to cells overexpressing HER2 *in vivo*, which method comprises administering a conjugate of said substance and a polypeptide according to claim 1 to a subject.

50. (Canceled).

51. (Canceled).

52. (Currently Amended) A method of detection of HER2 in a sample ~~according to claim 51~~, comprising the steps: (i) providing a sample to be tested, (ii) applying a polypeptide

according to claim 1 to the sample under conditions such that binding of the polypeptide to any HER2 present in the sample is enabled, (iii) removing non-bound polypeptide, and (iv) detecting bound polypeptide.

53. (Previously Presented) A method according to claim 52, in which the sample is a biological fluid sample, preferably a human blood plasma sample.

54. (Currently Amended) A method according to claim 52, in which the sample is a tissue sample, ~~preferably a human tissue sample, more preferably a biopsy sample from a human suffering from cancer.~~

55. (Previously Presented) A kit for diagnosis of HER2 overexpression in a tissue sample, which kit comprises a polypeptide according to claim 1 fused to a reporter enzyme, reagents for detection of activity of said reporter enzyme, and positive and negative control tissue slides.

56. (Previously Presented) A kit for *in vivo* diagnosis of HER2 overexpression, which kit comprises a polypeptide according to claim 1 labeled with a chelator, a diagnostic radioactive

isotope, and reagents for the analysis of the incorporation efficiency.

57. (Canceled).

58. (New) The method according to claim 54, wherein the sample is a human tissue sample.

59. (New) The method according to claim 54, wherein the sample is a biopsy sample from a human suffering from cancer.